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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

JiANG, DONG

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 09/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/904,462

Applicant(s)

ASHKENAZI ET AL.

Examiner

Dong Jiang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 July 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's preliminary amendment filed on 13 July 2001 is acknowledged and entered. Following the amendment, the original claims 1-38 are canceled, and the new claims 39-51 are added.

Currently, claims 39-51 are pending and under consideration.

Formal Matters:

Priority

This application claims priority to US provisional application 60/063,549, PCT/US98/19330, PCT/US00/04414, and US application 09/665,350. For the following reasons, the Examiner finds that the present claims 39-51 are not supported in the manner required by 35 U.S.C. 101 and 112, first paragraph by the prior applications, thus none of present claims is entitled to the benefit of the filing date of the prior applications.

US provisional application 60/063,549 filed on 28 October 1997 merely discloses a polynucleotide sequence of SEQ ID NO:1 or 2 (cDNA) encoding a polypeptide of SEQ ID NO:3, which is designated PRO229. The provisional application '549 fails to provide any specific, substantial and credible utility, and provides no guidance or working examples to teach how to use the claimed invention. Therefore, the Examiner is not able to establish that the priority document satisfies the utility/enablement requirement of 35 U.S.C. 101/112, first paragraph. As such, the claims of the instant application are not entitled to the benefit of the filing date of prior application US 60/063,549.

With respect to the latest priority application, US application 09/665,350, working examples are provided to support the utility of PRO229. However, the disclosure does not satisfy the utility/enablement requirement of 35 U.S.C. 101/112, first paragraph for the reasons addressed below under **Objections and Rejections under 35 U.S.C. §101 and §112**. Therefore, the claims of the instant application are not entitled to the benefit of the filing date of any of the claimed prior applications.

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Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

Specification and claims

The specification is objected to for the following informalities, appropriate correction is required: at page 106, line 5, it is unclear what is intended by "T cell surface glycoprotein *CD6* and *CD6*".

The ATCC accession number recited in claims 39-44, ATCC 209377, does not match that listed at page 250 of the specification, which is ATCC 209373 (for DNA33100-1159). Clarification and appropriate correction are required.

Applicant's attention is directed to 37 CFR 1.821. (d), which reads as follows:

Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Claims 31-48 are objected to for identifying a nucleotide sequence by a figure with SEQ ID NO: in parenthesis. The correct format to define a sequence structure is by referring to its SEQ ID NO. Correction is required.

Objections and Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 39-51 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a credible, substantial, and specific, or a well-established utility.

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Claims 39-51 are directed to an isolated polypeptide having an amino acid sequence of SEQ ID NO:148, % variants thereof, and a fusion protein thereof. The polypeptide is designated PRO229.

The specification discloses a human polypeptide, PPO229, having an amino acid sequence SEQ ID NO:148, which is encoded by a polynucleotide of SEQ ID NO:147. Based on sequence analysis, various portions of the PPO229 polypeptide have significant homology with antigen wcl.1, M130 antigen, T cell surface glycoprotein CD6, and it also is related to Sp-alpha, accordingly, the specification asserts that PPO229 polypeptide is a new member of the family containing scavenger receptor homology, a sequence motif found in a number of proteins involved in immune function and thus possesses immune function (page 106, the first paragraph, and page 22, lines 18-19).

The asserted utilities are not considered to be specific and substantial because the specification fails to disclose any particular function, and biological significance for the putative scavenger receptor of the instant invention. The speculation that the PRO229 would have potential functions similar to those of other known proteins based on sequence homology cannot be accepted in the absence of supporting evidence, because it is well known in the art that many proteins belong to a same family, yet have diverse, and sometimes even opposite biological activities and functions. For instance, dopamine receptor D1, a G protein coupled receptor, couples to Gs, and stimulates intracellular cAMP production upon binding to an agonist, whereas another family member, dopamine receptor D2 couples to Gi, and inhibits intracellular cAMP production upon binding to the same agonist. Additionally, Skolnick et al. (Trends in Biotechnology, 2000) teaches that because proteins can have similar structures but different functions, determining the structure of a protein may not necessarily reveal its function (see entire article, especially Box 2).

Therefore, the disclosed utility such as "immune function" requires additional knowledge about the claimed PRO229 before the protein can be used for any specific purpose. As virtually hundreds and thousands of molecules possess "immune function", the assertion that the PRO229 possesses immune function is clearly not specific and substantial. Additionally, "immune function" is a general term, and embraces many distinct biological properties. Therefore, even if the PRO229 possessed any "immune function", such description is not considered specific, and

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cannot be used to support an specific and substantial utility. Working examples regarding the biological property of PRO229 are noted (Examples 87 and 95), however, they are not sufficient to indicate a specific and substantial utility for the PRO229 for the following reasons:

In Example 87, "induction of c-fos in cortical neurons", treatment of cortical neurons with PRO229 polypeptide results in at least a 2-fold increase in c-fos mRNA by these cells (page 216, the last paragraph). However, the result is not considered substantial because it is known in the art that increased mRNA level does not necessarily correlate to an increase in protein production. For instance, Haynes et al. (Electrophoresis, 1998, 19: 1862-1871) studied 80 proteins relatively homogenous in half-life and expression level, and found no strong correlation between protein and transcript levels, for some genes, equivalent mRNA levels translated into protein abundances which varied by more than 50 fold, and Haynes concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript (page 1863, the second paragraph of the left column, and Figure 1). Further, even if the increased c-fos mRNA correlates to an increase in c-fos protein production, it is still unclear what is the biological significance of the PRO229 and increased c-fos in neuronal proliferation, which is asserted in the specification as that PRO polypeptide testing positive in this assay would be expected to be useful for the therapeutic treatment of nervous system disorders and injuries where neuronal proliferation would be beneficial (page 216, lines 31-32). The specification fails to provide evidence to illustrate the relationship between PRO229 polypeptide and a positive change in neuronal proliferation, which would support the assertion that PRO229 may be useful for the therapeutic treatment of nervous system disorders and injuries. As many proteins may regulate c-fos, one cannot extrapolate from increased c-fos that any protein, such as PRO229, inducing c-fos would be useful for treating nervous system disorders and injuries.

With respect to Example 95, a chondrocyte re-differentiation assay, the specification indicates that PRO229 polypeptide induces re-differentiation of chondrocytes, therefore, is expected to be useful for the treatment of various bone and/or cartilage disorders. However, there are no actual experimental results shown, or described in clear detail, such as what is the difference between positive and negative controls, to what stage the cell differentiated, and how many cells survived or dead in each group, and the specification merely defines a positive result as when the re-differentiation of the chondrocytes is determined to be more similar to the

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positive control than the negative control (page 235, lines 33-34). Although the PRO229 was tested "positive", as the result is ambiguous, one of skill in the art would not know how to interpret the significance of the result without more details to the critical questions mentioned above, therefore, would not know how to use the claimed invention based on that result.

Therefore, the disclosed utility for PRO229 polypeptide requires additional knowledge about the specific function and biological significance of the polypeptide before the protein can be used for a specific purpose, such as those set forth in the specification (pages 216 and 235). The specification does not provide sufficient information about SEQ ID NO:148. Upon further research, a specific, and substantial utility might be found for the claimed isolated polypeptide. This further characterization, however, is part of the act of invention, and until it has been undertaken, the claimed invention is incomplete.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-51 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial or credible utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Further, *even if* the specification taught how to use the PRO229 polypeptide, enablement would not be commensurate in scope with claims 39-51, which encompass % variants of SEQ ID NO:148 (claims 39-43, for example), and a fragment of the extracellular domain of SEQ ID NO:148 (claims 39-44, 47 and 48, for example).

The specification discloses *one* PRO229 amino acid sequence with particularity. No other PRO229 variants or fragments meeting the limitations of these claims were ever identified or particularly described. The specification does not teach how to use PRO229 variants or fragments. Since a biological function of PRO229 is not clear, and since one skilled in the art could not determine with a reasonable expectation of success what a biological function of

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PRO229 would be, the skilled artisan would not be able to make PRO229 variants or fragments, and test them for a biological activity. Furthermore, the specification provides no guidance as to how the skilled artisan could use an inactive PRO229 variant or fragment, as no functional limitation associated with the PRO229 variants or fragment in the claims. Therefore, it would require undue experimentation to practice this invention as claimed, because the skilled artisan would have no reasonable expectation of being able to use the PRO229 variants or fragments for any purpose stated in the specification.

Claims 39-51 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence, SEQ ID NO:148 (claims 39-43), or "the extracellular domain" of SEQ ID NO:148 (claims 39-44, for example). The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry,

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whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO:148, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. This is particularly important in absence of a specific known activity. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 39-44, 47 and 48 recite the "extracellular domain". However, the protein identified as PRO229 is a soluble protein, and is not disclosed as being expressed on a cell surface. Accordingly, the limitation that the claimed protein comprises the "extracellular domain" is indefinite, as the art does not recognize soluble proteins as having such domains. Further, if the protein had an extracellular domain, the recitation of "the extracellular domain ...",

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lacking its associated signal sequence" (claim 39, part (d), for example) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell.

The remaining claims are rejected for depending from an indefinite claim.

Rejections Over Prior Art:

The following rejections under 35 U.S.C. §§ 102 and 103 are made under the assumption that the effective filing date for the instantly claimed invention is 13 July 2001, which is the actual filing date of the instant application.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 39-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Wood et al., WO 99/14328.

Wood discloses a human polypeptide sequence (Figure 54), which is 100% identical to SEQ ID NO:148 of the instant invention (see computer printout of the search results). The cited sequence anticipates the present claims 39-49. Additionally, Wood teaches a chimeric molecule comprising said polypeptide fused to a heterologous peptide sequence, such as an epitope tag or a Fc region of an immunoglobulin (page 54, lines 14-17). Therefore, the reference anticipates claims 50 and 51.

Claims 39-44, 47, 50 and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Gebe et al., WO 98/39443.

Gebe discloses an amino acid sequence of a human Sp α polypeptide (Figure 1A-B), which comprises amino acid residues 1-346 of SEQ ID NO:2 of the instant case with 100% homology (see computer printout of the search results). The cited sequence anticipates the present claims 39-44 and 47 as being a polypeptide having the amino acid sequence of the extracellular domain of

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SEQ ID NO:148 (claim 1, part (c), and claim 47, for example). Additionally, Gebe teaches a fusion protein comprising said polypeptide fused to a murine immunoglobulin (the paragraph bridging pages 22-23, and Figure 4A), or an epitope flag (the figure at page 30). Therefore, the reference anticipates claims 50 and 51.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Gebe et al. (US 6,046,314) discloses a human Sp α polypeptide (SEQ ID NO:2) comprising amino acids 2-346 of SEQ ID NO:148 of the instant invention with 100% identity (see computer printout of the search results). Additionally, Gebe teaches a fusion protein comprising said polypeptide fused to a murine immunoglobulin (column 11, lines 46-48, and Figure 4A), or an epitope flag (column 15).

Kato et al. (WO 98/21328) teaches an amino acid sequence of a human polypeptide (SEQ ID NO:4), which comprises amino acid residues 1-346 of SEQ ID NO:2 of the instant case with 99.7% homology (see computer printout of the search results).

Conclusion:

No claim is allowed.

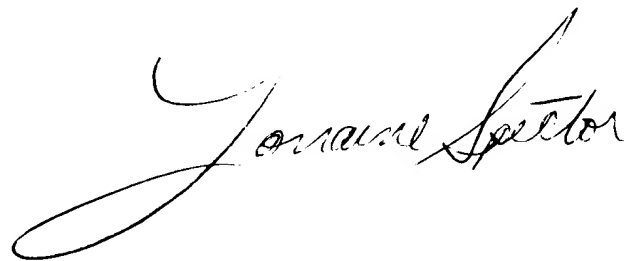
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Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

A handwritten signature in cursive script, reading "Lorraine Spector". The signature is written in dark ink and is positioned above a typed nameplate.

**LORRAINE SPECTOR
PRIMARY EXAMINER**

DJ
9/5/02